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## Transmission of infectious diseases through the placenta from mother to fetus

Ruth R. Burroughs  
*University of Nebraska Medical Center*

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Transmission of Infectious Diseases  
through the Placenta from  
Mother to Fetus

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A Review of the Literature

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Compiled by  
Ruth Reuben Burroughs

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Senior Thesis

1937

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University of Nebraska  
College of Medicine  
Omaha, Nebraska

480848

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Transmission of Infectious Diseases  
through the Placenta from  
Mother to Fetus

The placenta is generally defined as that organ within the uterus which establishes communication between the mother and the fetus. Besides its more truly physiological function, that of exchange of metabolic substances, the placenta has the power to prevent the passage of noxious substances on to the fetal circulation. This is spoken of as the "barrier" action of the placenta and is one of its important functions. But the placental barrier, though it is unquestionably of value and affords some degree of protection to the fetus in utero, is not insuperable. Besides many chemical poisonings, bacteria are known to pass from mother to fetus, the outstanding example being syphilis. (This disease will be omitted from our discussion because it is impossible in this short space to review the enormous amount of data available.) Before undertaking a discussion of the mechanism of transmission of the diseases to the fetus through the placenta, it is well to consider in general the anatomy and physiology of the placenta itself.

The essential construction of the placenta is that of a large glomerulus, a direct continuation of the dorsal aorta of the fetus. Frazer (31) says, "In the very young active organ there is an orderly arrangement of the vascular tree from the distribution of the main vessels in the fetal surface to their ultimate destination in the cotyledonous areas. There are numerous fine branches of both arteries and veins but a directness of blood supply through the cotyledons, a rapid return of fluids as well as an abundant anastomosis between the two placental arteries. In old placentae there is a marked lessening in number of the finer vessels, lack of compensatory circulation through lessening of anastomotic network, shrinkage of cotyledonous circulation with ultimate infarction in some areas." This infarction, a part of the ordinary senescence of mature placentae, seems to be a result of primary degeneration of the placenta and is significant in two respects: (1) It may result in injury to the fetus if very severe by limiting fetal blood supply, and, more significant to this discussion, (2) It may render the placenta susceptible to disease processes.

Physiologically the placenta may be considered as a permeable membrane falling into the third type in the classification of Höber (37), who describes permeable membranes as (1) sieve-like, those allowing permeation of substances if the holes are large enough, (2) solvent-like, those composed of a homogeneous layer of water-insoluble substance which allows permeation of substances soluble in the permeating layer, and (3) surface films, monomolecular in character and resembling sieves in structure but having some special properties in selective absorption not understood. In general, then, the placenta has the power of preventing noxious substances and infectious agents from crossing it. However, certain of these agents are able to permeate the normal placenta, especially if it be a mature placenta which has been weakened by normal infarction.

Until the work of Pasteur and Koch, knowledge of transfer of infection was gained by inference and hypothesis. In 1900 Dorland (24) presented two theories in explanation of placental transmission, the parasitic and leucocytic. The parasitic theory assumes that bacteria cause destruction or fibrous degeneration of the epithelium of the placental villi and change or abolish its selective power. The leucocytic theory assumes that normal placentae contain disease-resisting leucocytes which protect the fetus, but if these placental leukocytes are overcome or develop originally in a diseased uterus, they will aid in transmitting disease to the infant. Dorland leaned toward the first or parasitic theory. Recent research by McLean (51) bears him out. McLean found that filtrates from certain bacteria contain a soluble factor that increases the permeability of tissues and enhances the infections produced by these organisms. This diffusion factor was found in filtrates of *Cl. welchii*, *Cl. chauvei*, and *Vibrio septique*, and in virulent strains of type I pneumococcus. He found a small amount in *C. diphtheriae*.



It is also possible that organisms may force their way through the placenta by their own motility and may even exert no effect on the placenta. Spirochetes, for example, have been found pierced halfway through the chorionic layer of the placenta and in the villous stroma without any evidence of local tissue change (Kearns (42)). Alpers and Patten (3) believe that the typhoid bacillus may also be transmitted by its own motility.

It is obvious that organisms must be present in the maternal blood or lymph stream or exist in the uterus itself before it is possible for them to pass through the placenta. Doubtless the ability of organisms to invade and persist in the maternal blood is a factor of great importance. The size of the infecting organism is not an important factor according to Adair (1), as the large spirochete passes through with ease, unless, as Adair and others have suggested, there is some undiscovered precursor that may transmit syphilis.

It is important to understand clearly the criteria used in determining that transmission of disease

through the placenta has taken place. Cases in which the infant was born dead, either prematurely or at term, with bacteriologic or pathologic evidence of disease similar to that of the mother are regarded as cases of true transmission. The few cases of infants born alive with positive clinical evidence of disease may also be included. It must be remembered that although the child dies and is aborted during an acute infection of the mother, that child is not always infected but may die from the uterine contractions stimulated by the high temperature or from the hypercarbonization of the blood in those diseases which are attended by cyanosis, for example, pneumonia (De Lee 22). In such cases the pathologic and bacteriologic evidence is lacking in the child. Bacteriologic findings alone must also be viewed with suspicion, since, according to Kobak (43), a fetus may have a temporary bacteremia of unknown origin without ill effects. In fact 34, or 9 per cent, of his 374 routine blood cultures in newborns were positive for bacteria.

There are many reported instances in which the

disease from which the mother suffered developed in the infant several days after birth. While these have been accepted by others as evidence of transmission of disease, caution must be used in so considering them, for the possibility of infection during or immediately after birth cannot be easily dismissed, despite the fact that the infant had been removed from the mother.

### Tuberculosis

The first report of intrauterine transmission of tuberculosis was made by Schmorl and Birch-Hirshfeld (63) in 1891. In their case the mother died of tuberculosis, the lungs showing extensive evidence of the disease, both miliary and otherwise. Tubercle bacilli were found in the placenta, and inoculation of guinea pigs with the fetal liver, spleen, and kidney revealed widespread evidence of the presence of tubercle bacilli, although there was no outward sign of tuberculosis in the fetus. Birch-Hirshfeld believed the mode of transmission of the bacilli was by "growing through the placenta as in the case of anthrax."

Also in 1891 a case was reported by Saboraud, quoted later by Alpers and Patten (3), in which autopsy on an eleven day old infant born of a tuberculous mother showed miliary and large tuberculous nodules in liver and spleen. The mother had died at delivery. Weber (71) in 1916, after an extensive survey, called attention to the fact that in fetuses and very young children the localization of tuberculous change is in the liver and lymphatic glands, especially the

portal, bronchial, and mediastinal, a fact suggesting the umbilical vein as the portal of entry of the organism.

The earlier reported instances were listed by Dubois (25) whose survey of cases shows that death took place from one to eighty-nine days after birth of the child--long enough, we believe, for many of the infants to have contracted tuberculosis during or after birth. Ballantyne (6) felt that many kinds of infection are "transmitted from the mother showing itself in similar form in the fetus" but among such transmissions tuberculosis occurred very rarely. Hess (36) in 1922 stated, "In comparison with acquired tuberculosis the congenital form is almost a rarity, taking place when a bloodvessel of the villus becomes eroded or ruptured and allows passage of bacilli into the fetal blood." Adair (1) also states that "tuberculosis is rarely seen in the fetus", and Cumston (18) feels that such infection must be rare occurring only with a bacteremia of the mother at term when uterine contractions squeeze the bacilli into the fetal circulation.

Whitman and Greene (73), after collecting all cases of congenital tuberculosis reported up to 1922, reach an opposite conclusion: "Whatever facts may ultimately prove to be, there is already sound reason for believing that prenatal infection is an important, if not the most important, method of propagating the disease." The tabulation of 113 authentic cases and 519 doubtful cases given by these workers is here reproduced:

	Authentic	Doubtful
Congenital tuberculosis of		
fetus and placenta	38	509
Tubercle bacilli but no histologic		
changes		
Fetus and placenta	21	10
Fetus only	3	....
Same in fetus with histologic		
tubercles in placenta	4	....
Tuberculosis of placenta, with bacilli		
and histologic changes	44	....
Bacilli, but no histologic tubercle,		
placenta only	3	....

In general, as stated by Hess and by Adair and Steiglitz (2), transmission occurs when there are active lesions in the decidua and placenta which enable the bacilli to penetrate into the fetal blood stream. Couvelaire and Lacomme (17) are of the opinion that transmission is more likely to occur when the mother has a fatal form of tuberculosis such as tuberculous meningitis in which a very virulent organism is in the blood stream.

It is possible that this disease may pass from the blood of the mother to the fetus without producing disturbance of the placenta. Monckeberg and Vergarak (52) found that blood from the cords of three out of four infants whose mothers had tuberculosis when injected into guinea pigs produced pulmonary tuberculosis. Moreover, in a study of ten stillborn infants from tuberculous mothers, Calmette, Valtis and Lacomme (14) found that extracts of various organs and glands of these infants would produce tuberculosis in guinea pigs although no lesions at all appeared in the infants or in the placentae.

The question has been raised as to whether one

cannot suppose that the fetus may be a carrier of a filterable form of tubercle bacillus received from its mother in the course of uterine life, and that such virus may be inactive for a long period of time. Couvelaire (17) recognizes the possibility of transplacental infection by a filterable virus and feels that it may be of considerable significance. Rather strong argument against this theory is the fact that large numbers of infants removed from tuberculous surroundings at birth do not become tuberculous. The positive tuberculin test reported by Krause (45) occurring uniformly in infants of tuberculous mothers is not indicative of transmission of the disease, he says, but only of tissue allergy to the tuberculo-protein.

It is difficult to say finally how important is placental transmission of tuberculosis. Without doubt it does occur, but in all cases studied and presented the infant was either stillborn or died shortly after birth. Is it possible that some infants with unrecognized tuberculosis escape death at birth but develop it at some later time, as suggested by Whitman and Greene, or is the death of the tuberculous infant at



or before birth almost certain?

### Infection with Streptococcus and Related Pus-Forming Organisms

In 1886 Lebedeff (46) reported an instance in which a pregnant mother with erysipelas of the lower extremities gave birth to a full term infant who lived for ten days and who showed in many places a loss of the epidermis, hemorrhages and lymphocytic infiltration in the dermis. Streptococci were found in the fatty tissue of skin and umbilical cord. Dorland (24) in 1900 cited cases of apparent transmission of streptococci. DeLee (27) in 1919 reported a positive culture of streptococci viridans from the heart and spinal cord of a macerated fetus whose mother died of heart disease.

In 1915 Slemons (66) stated that, although he believed organisms did pass through the placenta to the fetus and could be demonstrated in both, they arrived in the placenta rarely from maternal blood but more commonly after ascent from the vagina and cervix and primary infection of the amniotic fluid.

This theory seems applicable to certain other of DeLee's (20) cases in which infants dying before or at birth showed organs filled with virulent bacteria, streptococci or pneumococci, and in which the illness of the child seemed to be independent of the mother, the mother being only indirectly affected or not diseased at all.

Another theory, that of focal infection in the mother with localization in the placenta and subsequent transmission to the fetus, might be used to explain these last cases of DeLee as well as certain other cases here to be presented. Curtis (19), for instance, treated successfully several cases in which focal infections with a tendency to fresh exacerbations or repeated oral cavity infections of the mother appeared to be an important cause of otherwise inexplicable spontaneous abortion in women. In his cases hemolytic streptococci found in the fetal organs and injected into pregnant rabbits caused infection of the uterine cavity and of the embryos. A similar case of streptococcus infection with confirmatory bacteriologic and experimental findings was reported by Browne and

Kincaid (13) whose case was that of an apparently well mother being delivered at seven months of a macerated fetus from whose heart blood a virulent hemolytic organism was recovered.

Kramer and Wright (44) felt that each virulent organism had a predilection for certain tissues or organs and they cite a case in which autopsy on an eight months fetus removed from the uterus of a woman who died of streptococcic meningitis showed purulent exudate over the base of the child's brain. Streptococci of the same type as those found in the mother were isolated.

Dunham (26) in 1933 reported thirty-nine cases of septicemia in newborns due to various organisms. In eight cases symptoms were present at birth, in four others they appeared on the first day while in twenty-eight out of the thirty-nine, they appeared within two weeks. In three cases the cultures of the mothers' blood were also positive. The type of infection in the mother varied, including septicemia, umbilical and cutaneous infections, among them erysipelas. The organisms were streptococci in 15 per cent of the

cases and staphylococci, pneumococci and colon bacilli in the remainder. Although many of Dunham's cases must have been postnatal in origin, a few were undoubtedly instances of transmission in utero.

D'Ewart (23) in 1931 demonstrated at postmortem examination of a thirteen day old child an endocarditis caused by staphylococci which he believed followed a septic condition of the cord and was possibly transplacental in origin. Hemsath (35) in 1936 found "groups of intracellular and extracellular gram-positive cocci and diplococci in pus from the middle ear" of his several cases of stillbirths, but he considered transplacental infection improbable in middle ear infections. His belief was that amniotic fluid contaminated by infectious material from the birth canal was swallowed or aspirated by the fetus and somehow entered the middle ear cavity to set up an inflammation.

An unusual case of prenatal colon bacillus infection was presented by Alpers and Patten (3) in a child delivered two months prematurely by Caesarian section and dying nine days later, at which time cultures of material from the middle ear and meninges revealed *B. coli*.

The number of authentic cases of transmission of pyogenic infections, as can be seen, is not great although there are many clinical reports. In a general summary given by Alpers and Patten it is stated, "The infection is usually in the maternal blood stream and is almost always fatal to the mother as well as to the fetus."

#### Scarlet Fever

Scarlet fever is now generally considered to be caused by a streptococcus and so will be discussed here as a supplement to the discussion of streptococcic infections. In 1893 Ballantyne and Milligan (7) reported a case in which the onset of symptoms of scarlet fever occurred in an infant the day after birth, desquamation occurring later simultaneously with that of the mother. Authentic cases similar to this one had been reported even earlier by Walker (70) in 1880, Saffin (61) in 1886, and DeLee (21) in 1892. DeLee's case was one in which, two weeks after exposure of the mother to scarlet fever, she was delivered of a child found to be desquamating freely over the whole of the

trunk and limbs. An almost identical case was presented in 1916 by Liddell and Tangye (48). In their case the mother had had scarlet fever previously and did not herself become sick except that during the week before delivery she complained of a "burning pain inside". Alpers and Patten (3) cite several other cases which leave no doubt that scarlet fever is transmitted during intrauterine life.

#### Pneumococcic Infection

We feel definitely able to prove that pneumococcic transmission, though not frequent, does take place. Early instances were reported by Thorner (quoted by Strachan) in 1884 and by Strachan (67) in 1886 whose case was that of a premature infant who, after death on the first day, showed an acute pneumonic consolidation of the whole left lung. Dorland (24) in 1900 also cited cases to prove placental transmission of pneumonia. Becardit (9) described a case of severe grip with pulmonary complications occurring in a woman delivered of a child at term. Both infant and mother died in twenty-four hours,

autopsy revealing pneumonia in both lungs of the mother and cocci were cultured from the blood of mother and fetus.

Hess (36) says, "That congenital pneumonia may exist seems to be well substantiated, although the number of cases reported in which the infection was hematogenous and transmitted by way of the placenta is small." Browne (11 and 12) considered pneumonia and other infections as received only during or after labor. Johnson and Meyer (40) reported in 1925 a series of cases of pneumonia due to antenatal infection and consider the disease an exceeding frequent cause of mortality in stillborns and newborns. A majority of their cases, however, were apparently due to aspiration of amniotic fluid following infection of the amniotic sac after premature rupture of the membranes. They admit the possibility of transplacental infection but felt that they could not so classify any of their cases.

Gordon and Lederer (32) reported the death of a three day old infant whose mother suffered from pneumonia and delivered in the eighth month. Autop-

sy on the child revealed extensive pneumonia, empyema, and pneumococcemia. Another report, that of a child delivered at term but dying on the fourth day and showing at autopsy evidence of extensive fibrosis of the lung and intrauterine pneumonic infection in the process of healing, was made by Anderson and Pohl (4). The mother had had a mild pain in the chest and cough during the fifth month of gestation. Cornell (16) had a similar case.

Rare instances of pneumococcic meningitis in the newborn have been reported, but proof of intrauterine transmission is not conclusive. Only in the last few years have cases been reported. Heinz (34) in 1928 reported a case in which a mother acquired pneumococcic meningitis before delivery, and her infant showed signs of meningitis on the eleventh day and died on the twelfth. Type I pneumococci were recovered from both. Uhr (69) diagnosed pneumococcic meningitis in a child who developed symptoms on the fifth day. His case was treated only by lumbar puncture and recovered. Coppolino and Gannone (15) presented a case in which the mother, suffering from "grip", delivered



a child who from birth showed no signs of the activity of the normal infant and whose spinal fluid showed pneumococci on the third day.

In none of the cases of pneumococcic meningitis here presented could a post-natal infection be entirely excluded. Transmission of true pulmonary pneumococcic infection, on the other hand, cannot be doubted in several of the cases presented.

#### Typhoid and Paratyphoid Fevers

Ballantyne cites typhoid fever as one of the diseases transmitted from the mother and causing fetal death.(6). The first report of transmission of this disease was made by Eberth (27) in 1889. He found typhoid bacilli in the liver and spleen of a six month fetus born of a mother suffering from typhoid fever. In 1892 DeLee (21) also demonstrated typhoid bacilli in the spleen of a five month fetus from a similar case.

Dorland (24) reviewed a number of cases from the literature of delivery of premature or stillborn infants during a typhoid attack on the mother. Cultures

of typhoid bacilli were made from the fetal organs. He says that typhoid fever during pregnancy will cause abortion in sixty-three per cent of cases. In many of the fetuses bacilli can be found without any macroscopic lesions. Death of the child, he believes, is due to acute blood poisoning before local change could occur.

"The complication of typhoid with pregnancy occurs in 1.2% of all cases of typhoid or in one in thirty thousand births," are the statistics of Alpers and Patten (3). "In most instances the result is a premature or dead fetus. Viable fetuses have a poor prognosis. The disease is transmitted through the bloodstream, the mother usually suffering from typhoid septicemia. Because of the motility of the bacillus it may pass the placental membrane without leaving evidence of its presence."

Cases of transmission of paratyphoid are exceedingly rare. In 1912 Yamada and Doi (76) reported the presence of paratyphoid B bacilli in the bladder, spleen and heart blood of a one and a half months fetus whose mother had a similar infection. Schmidt (62)

presented a case of an apparently normal child born of a mother with a paratyphoid B infection. Cultures of the blood and stool of the child revealed the same organism in the child as in the mother.

### Anthrax

In a small number of cases anthrax seems to have passed across the placental membrane. In 1900 Dorland (24) cited a few cases from the literature which tended to prove such transmission. Alpers and Patten (3) in 1936 presented a fairly extensive review, which is summarized here. Eppinger,<sup>(28)</sup> they state, noted anthrax bacilli in the chorionic villi of a mother who suffered from the disease. Since no evidence of the infection was observed in the fetal blood or organs, this can hardly be considered a conclusive case. In Paltauf's (54) case the bacilli were recovered from the lungs of the fetus. Rostowzew (59) reported three undoubted instances of transmission of the disease. In a woman of thirty-four with a malignant pustule of the left cheek, the bacilli were observed in the liver, spleen, pancreas, kidneys, bladder and mesenteric

lymph nodes. They were present in the placenta and in the liver of the fetus also. The second patient was a woman of thirty-six with a malignant pustule of the right cheek. Anthrax bacilli were present in the mother's liver, spleen, kidneys, stomach, uterus and heart, and in the fetal liver, spleen, kidneys, and adrenal glands. The third case occurred in a woman with a malignant pustule of the lower lip, who had anthrax bacilli in the liver, spleen, kidneys, lungs, bladder, and cerebral cortex. The bacilli were present also in the liver and adrenal glands of the fetus. Hofman (38) noted pathologic changes and bacilli in the placenta of a patient with anthrax infection. Birch-Hirshfeld (63) felt that anthrax bacilli "grow through the placenta".

Although clinically there is little doubt that anthrax is transmitted from mother to fetus, Wolff (75) was unable to find anthrax organisms in 17 cases of guinea pig and rabbit fetuses from infected mothers.

In every case reported of anthrax transmission, the result to the fetus has always been fatal.

### Cholera

There is much doubt about the transmission of cholera to the fetus. The only reported case is one in 1888 by Tizzoni and Cattani (68) which concerns a woman of twenty-six in whom typical cholera developed during her fifth month of pregnancy. She was delivered of a dead fetus at that time. Cultures of the blood, transudates and intestinal contents of the fetus revealed the typical cholera bacillus. Sellards (64) states that cholera usually causes abortion. Brought on by cramps in the uterus similar to the cramps in the other muscles, this abortion occurs before infection could take place. Moreover, the spirillum of cholera usually remains at the source of infection in the mucosa of the colon and does not cause a bacteremia or subsequent deposit of organisms in the placenta. Therefore transmission of this disease does not seem likely.

### Gonococcic Infection

Transmission of this disease is claimed in several instances. Alpers and Patten (3) give a review of all

cases reported up to 1936 and quote cases of Fischer, Knauer, Slobozianu and Herscovici, and others, in each of which the child was delivered by a mother suffering from acute gonorrhea or from gonococcic arthritis, and in which the child developed joint involvement some time after birth. Cultures or smears of the joint fluid were positive for gonococci in all cases.

Royston's (60) case was also one in which joint involvement occurred. The mother had arthritis of the wrist, shoulder, knee, and ankle joints from which a pure culture of gonococci was recovered. On the fifth day after birth the child developed swelling of both wrists and the left knee. Gonococci were recovered from the joints.

In none of these cases was the evidence of transmission through the placenta conclusive. In all reported cases the disease developed sufficiently long after birth to be attributed to postnatal rather than to prenatal infection.

### Malaria

The only propozoan disease in which transplacental infection is claimed is malaria, and even in this disease the subject is much debated. It is said that Hippocrates was familiar with malaria in the newborn and considered it congenital in some cases. Johnstone (41) states that "normally there is no passage of maternal blood cells to the fetal blood nor do large parasites like that of malaria pass through the placenta.

Blacklock and Gordon(77) had a series of 162 cases in each of which the mother had malaria. In no case were parasites found in the blood of the umbilical cord although 38 per cent of the placentas were positive for protozoa. Strangely, no crescents were found in the placentas showing that the infective organisms were not reproducing in the site. These authors say that the frequent fetal death in malaria is due to severe destruction of erythrocytes in the umbilical cord by toxic substances absorbed from the infected placenta and is not due to malarial infection.

In 1910 Beekel (10) reported a case of malaria in

a seven week old child occurring in Cleveland, which is not a malarial district. Beekel reviewed the literature to 1910 quoting twenty authorities and found twelve cases of indubitable placental transmission. Since 1910 at least 15 conclusive cases have been reported. Bass (8) reports a case occurring in mid-winter in New York City in a four week old baby whose mother had a tertian infection during the fifth month of pregnancy. Postnatal infection is excluded by Bass on account of the season and location.

Forbes (30), working in a dry climate (Colorado) where anophales mosquitoes are never found, reported a typical quartan malaria developing in a child seven weeks old whose mother had had malaria of similar type seven years before. Peters (55) in 1902 diagnosed malaria in a child born in Baltimore of a mother who suffered from malaria. The child developed symptoms shortly after birth and parasites were found on the fiftieth day.

Along with these occasional reports must be quoted a study by Weselko (72) in 1926. He reported two hundred cases of congenital malaria, in 187 of



of which there were positive blood findings. In many of these cases the parasites were not seen in the blood immediately after delivery, but appeared a little later. Wickramasuriya (74) in 1935 presented six cases in which evidence of transplacental transmission seems definite. In his cases the maternal infections were very severe. He concludes that intra-uterine fetal infection with malaria occurs more often than is supposed, and that it occurs chiefly in severe and in untreated cases of malignant tertian infection. Owing to the sluggish circulation in the intervillous spaces and to the barrier action, the parasites tend to be aggregated and arrested in the placenta. The intense infection of the placenta with parasites and the accompanying high temperature may cause either premature separation or injury of the placenta, permitting at least some of the parasites to cross the barrier. Proper treatment, reducing the number of parasites in the placenta, probably explains why the fetus escapes so often in severe infection.

It has been suggested that in those cases in which a newborn child does not show symptoms of malaria and

in which parasites are not found in the blood for a few weeks, a latent type of malaria is present. This idea is held by Forbes (30) and others. Blacklock and Gordon (77) deny this supposition and maintain that this so-called latent period is merely the time before postnatal infection occurs.

It appears after a review of all these cases that placental transmission of malaria does occur, but after considering the great number of cases of malaria in pregnant women and the very few reports of transmission, we may assume that such transmission may depend on some abnormality or accident of gestation, as described earlier.

### Measles

The earliest cases of congenital transmission of measles are said to be those of Fabricius Hildranns (1616) and of Ledelius (1685). A review of the literature up to 1893 is given by Ballantyne (5) who states that trustworthy accounts of transmission of measles are rarely possible since few pregnant women contract measles. Ballantyne's case was one in which the mother contracted measles during the sixth month of her pregnancy and delivered a premature infant which presented a typical rash of measles. A similar case was reported in the same year by Robinson (57). Alpers and Patten (3) reviewed a few other cases reported up to 1936.

It is difficult to decide in many cases if transmission of measles has occurred in utero. The disease in all probability occasionally runs its course in utero and has disappeared before birth. On the other hand, infection may take place in utero, but the rash may develop late enough to be called postnatal. Reports of definite cases in which the rash is present at birth are few.

## Varicella

Only two authentic cases of infection of the infection of the child in utero with chicken pox have been reported. Pridham (56) in 1913 saw a child four hours after birth who presented a rash over the entire body identical with that seen on or about the fourth day of varicella. There had been a history of exposure of the mother fourteen days before, but she had not contracted the disease herself.

Grindon (33) in 1932 reported a case in which a mother just recovering from varicella delivered a full term baby on whose face, left arm, back and buttocks were a few typical lesions of chicken pox.

These cases are too few in number to allow any conclusions to be drawn from them.

## Variola

Variola is one of the few diseases conceded by every author as transmitted through the placenta. As early as 1702 Duttel, it is claimed, knew something of the relation of variola to pregnancy and to the fetus. John Hunter observed the passage of variola from mother

to fetus, and Mauriceau, it is said, was born with healed cutaneous lesions of smallpox.

Epstein (29) divides the reported cases of variola in the newborn into four groups: 1. Those in which the mother was healthy and fetus infected. Here there is possibility of infection ascending through the birth canal to reach the fetus. 2. Those in which variola in pregnancy was followed by abortion. In this group the fetus showed no signs of variola and died without acquiring the disease. 3. Those in which there was variola in both mother and fetus. In many cases the infection had run its course in utero, and the infant was born with only scars or traces of variola. 4. Those in which variola of the mother was followed by birth of an infant at full term, the infant later acquiring the disease. In those cases in which the eruption occurred in the first day or two after delivery, there can be no doubt that transplacental transmission occurred. Numerous cases have been reported in each of these groups.

As early as 1888 Simpson (65) stated, "We have occasional illustrations of the death of the intra-

uterine foetus from Acute Disease during certain epidemics..... We may have a woman seven months pregnant, for example, passing through an attack of modified small-pox, and three weeks later, after the fever has subsided, she may give birth to a dead foetus with pustules all over the body, and the placenta giving no evidence of pathological disturbance."

Lynch (47) reviewed a number of cases presented up to 1932 in which dead fetuses showed scars of variola. Moreover, in numerous cases, some of them this author's own, the pregnant woman has been vaccinated and her child delivered showing lesions of vaccinia.

Variola is a serious complication of pregnancy causing high mortality in both mother and child. Death of the fetus occurs occasionally from the infection, but it is more generally due to the high temperature and the toxemia coincident with the infection.

#### Miscellaneous Virus Infections

McGoogan (50) in 1932 discussed the possibility of placental transmission to the fetus of the virus of acute anterior poliomyelitis, and quoted several

authors (Mercier, Marinesco, Jorge and Levaditi) who believed such transmission did occur and who presented their cases as proof. McGoogan himself rather doubted that such a transmission ever did occur although he admitted its possibility.

Another virus disease affecting the central nervous system is epidemic encephalitis of which Roques (58) says, "There is evidence both pathological and clinical to show that the virus is capable of making its way across the placenta, and that, therefore, some of the reported cases have become infected before birth." Such transmission is certainly indicated in the case he cites in which clinical signs similar to those exhibited by the mother were seen in the child at birth or immediately afterwards. Patterson and Carmichael (53) report the cases of two siblings who showed symptoms referable to the central nervous system just after birth. The mother had had encephalitis lethargica twelve years before; autopsy on the children at six months and two years of age respectively showed evidence of infection of the brain tissue somewhat similar to encephalitis lethargica. No

organisms were found.

Both of these diseases occur so rarely during pregnancy that the effect on the fetus cannot be accurately judged.



1. The normal placenta is so arranged that there is no entrance of maternal blood into the fetal circulation. The "barrier" between maternal and fetal circulation has in most cases also the power of preventing passage of noxious substances to the fetus, but this barrier, although of unquestionable value, is not insuperable.
2. Placental transmission probably depends on some damage to the epithelium of the placental villi which so changes or abolishes its selective power that infectious agents pass through. In some cases bacteria such as the spirochete of syphilis or the typhoid bacillus may force their way through an unbroken placental membrane by their own motility.
3. Cases in which the infant was born dead, either prematurely or at term, with pathologic or bacteriologic evidence of disease similar to that of the mother are the only ones which can be regarded without suspicion as cases of true transmission.
4. Diseases which seem definitely to be transmitted (with the exception of syphilis) are:

a. Certain bacterial diseases.

Tuberculosis. Transmission of this disease seems to depend on (1) some erosion of the villous epithelium to allow passage of the bacillus, and (2) presence of the bacilli in the maternal blood stream.

Streptococci, and other pus-forming organisms. These may be transmitted if the infective agent is in the blood stream of the mother. In any case the child usually dies. The prognosis in the mother is also poor except in a few cases in which a "focal infection" with localization in the fetus seems to occur.

Scarlet Fever.

Pneumococcic infection. Transmission has been proved by the vast numbers of cases. The mechanism of transmission is not known. Pneumococcic meningitis is not definitely known to be acquired by the fetus through the placenta.

Typhoid and paratyphoid fevers. Since these cause a bacteremia in the mother they can and do easily invade the placenta and are transmitted. Penetration of the placental villi may be due to the motility of the organism.

Anthrax. This organism probably grows through the placenta to infect and generally to destroy the fetus.

b. One protozoan disease, malaria, which can, but usually does not infect the child of a malarial mother unless she is suffering from a severe type of infection.

c. Certain virus diseases

Measles. A few conclusive cases are presented.

Variola. This disease is the only one besides syphilis which all authors concede to be transmitted by the mother to her intrauterine child.

5. Cases have been presented to suggest transmission of cholera, gonococcic infection, varicella, acute poliomyelitis and epidemic encephalitis, but the literature is so lacking in confirmatory findings that no definite conclusions can be drawn concerning the transmission of these diseases.

It must be admitted that certain diseases other than syphilis may be transmitted through the placenta to the fetus. The importance of such a transmission in the case of syphilis has been thoroughly emphasized, and important steps have been taken to prevent the infection of the fetus. However, little has been said of the significance of transmission of other diseases.

It is probably true that congenital infections usually cause death of the child, and such deaths are more common than is generally thought. Holland and Lane-Claypon (39) in 1926 classified causes of death in fetuses and showed that, excluding syphilis, almost fifty per cent of fetal deaths are due to infections of various kinds.

How many infants survive, although infected antenatally, is not known because infection in newborns is rarely diagnosed. Although bacteria may be found in microscopic or bacteriologic examination if search were made, the infectious diseases as a rule do not manifest their characteristic visceral lesions in the fetus, probably because of the passivity of these organs during antenatal existence. Can it not be conceived

that the child may live to show symptoms later on of disease, such as tuberculosis, or may it not show damage, as to the brain, from the scars of old healed inflammation?

Although no specific remedy can be offered to prevent this fetal infection, there is some chance that if medical men and lay individuals were aware of the dangers of exposure to contagious disease by the pregnant woman, that some reduction could be made in fetal mortality and in the possible morbidity which may cause indeterminable handicaps in the later life of the child.

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